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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,983	01/04/2005	Yasuhiro Kajihara	ACT-001	3218

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EXAMINER	
BLAND, LAYLA D	

ART UNIT	PAPER NUMBER
1623	

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06/17/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,983	KAJIHARA, YASUHIRO	
	Examiner	Art Unit	
	LAYLA BLAND	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-7 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-7 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is a response to Applicant's amendment submitted April 7, 2009, wherein claims 1 and 7 are amended.

Claims 1, 5-7, and 22-25 are pending and are examined on the merits herein.

In view of Applicant's amendment submitted April 7, 2009, the rejection of claims 1, 5-7, and 22-25 under 35 USC 112, second paragraph, for indefiniteness with respect to the fat-soluble protecting group recited in steps 6 and 7 of claim 1 is withdrawn. Step 6 has been amended to recite that the amino group nitrogen is protected with a fat-soluble protecting group.

The following rejection of record is maintained:

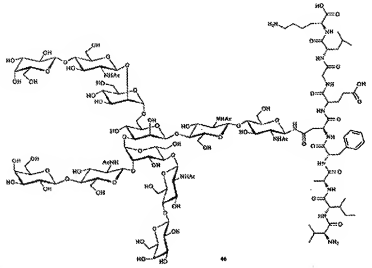
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5-7, and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meinojohanns (J. Chem. Soc. Perkin Trans. I, 1998, pages 549-560, PTO-1449 submitted December 20, 2007) in view of Komba (Journal of Peptide Science, 6: 585-593 (2000), PTO-1449 submitted December 20, 2007) and Ratcliffe (US 5,527,901, June 18, 1996, of record).

Meinojohanns teaches a method for preparing N-linked glycopeptides such as the one shown below [page 556, Scheme 5]:



The products can be prepared by attaching an Fmoc-protected amino acid to a resin, followed by deprotection of the Fmoc group and coupling of another amino acid, which is repeated. Then the asparagine building blocks, which are protected with Fmoc as well (see page 555, Scheme 4), are coupled and the peptide synthesis is continued as described above. Finally, the glycopeptide is cleaved from the resin. [pages 559-560]. Secreted and cell-surface proteins are glycosylated with both N- and O-linked oligosaccharides, and the effects of the sugars on such properties as immunogenicity is of importance [page 549, first paragraph]. The N-linked glycopeptides prepared by Meinojohanns could be used as substrates for 1-6-sialyltransferase [page 556, scheme 5].

The difference between Meinojohanns' process and the claimed process is that Meinojohanns does not utilize an asparagine-linked oligosaccharide containing a sialyl

moiety which is protected with a benzyl, allyl, or diphenylmethyl group, but instead suggests the use of sialyltransferase to introduce sialyl moieties.

Komba teaches the preparation of Sialyl-T-Glycopeptides (which are O-linked as opposed to Meinojohanns' N-linked glycopeptides). The products were prepared via the Fmoc/OPfp-ester strategy, as shown below [page 590, Figure 1]:

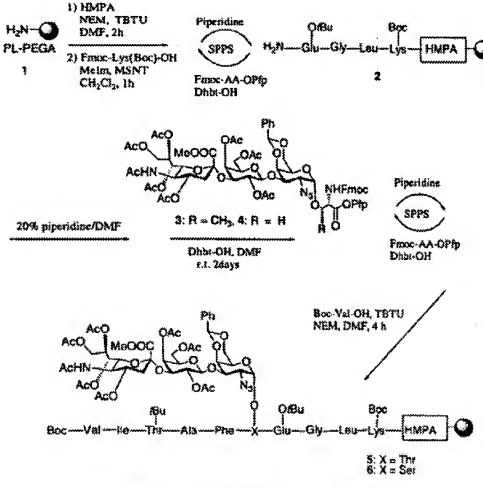
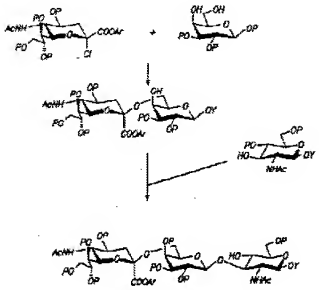


Figure 1 Solid-phase glycopeptide synthesis.

The glycopeptides were cleaved from the resin before deprotection of sialic acid, because the free carboxylic acid on the 1-position of sialic acid rendered the glycosidic linkage more susceptible to cleavage [page 590, first paragraph].

Ratcliffe teaches a method for preparing sialic acid glycosides, using sialic acid protected by an aryl group, as shown below [see abstract].



Sialic acid glycosides occur in complex oligosaccharides attached to proteins [column 1, lines 57-59]. Synthetic strategies for higher sialosides typically use a methyl ester as a blocking group for the acid moiety, but the use of methyl ester results in limitation of subsequent use of the product, because it is difficult to deblock the sialoside while maintaining other ester groups [column 2, line 55 – column 3, line 5]. Benzyl or phenacyl ester blocking groups give a higher yield of product and higher anomeric purity [column 4, lines 1-7].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to carry out the method of Meinojohanns using sialylated oligosaccharides, wherein the sialic acid group is protected with a benzyl or phenacyl group. The Supreme Court in KSR reaffirmed the familiar framework for determining

obviousness as set forth in Graham v. John Deere Co. (383 U.S. 1, 148 USPQ 459 (1966)), but stated that the Federal Circuit had erred by applying the teaching-suggestion-motivation (TSM) test in an overly rigid and formalistic way. KSR, 82 USPQ2d 1385. Exemplary rationales that may support a conclusion of obviousness include use of known technique to improve similar devices (methods, or products) in the same way. In this case, use of a known technique to improve a similar method in the same way would lead the skilled artisan to the claimed invention. The claimed invention can be seen as an improvement over the method of Meinojohanns because the sialyl group is present without requiring additional enzymatic transformation. However, Komba teaches a method wherein the sialyl moiety can be introduced chemically, attached to the oligosaccharide, via protection of the acid group. One of ordinary skill in the art could have applied Komba's technique to Meinojohanns' method and would have expected the modification to be successful, because the two methods are otherwise quite similar.

Using a different rationale, there was a teaching in the Meinojohanns reference that suggested the use of sialyltransferase, a teaching in the Komba reference regarding the importance of sialyl groups in glycopeptides, and a teaching of how to prepare sialylated glycopeptides. Thus, the skilled artisan would be motivated to prepare sialylated derivatives of the Meinojohanns glycopeptides, and could use the Komba method to do so.

It would have been further obvious to one of ordinary skill in the art to carry out the method, as described above, but using benzyl protection in place of methyl

protection for the carboxyl group of sialic acid. Komba teaches the use of the methyl ester. Ratcliffe teaches that the benzyl ester is an alternative to the methyl ester for protection of the carboxyl group of sialic acid, and offers benefits such as more effective removal in the presence of other blocking groups, higher yields, and higher anomeric purity. Thus, the skilled artisan could have employed the benzyl ester in the method as described above, and would have expected the method to be successful.

Response to Arguments

Applicant argues that the Ratcliffe reference is of a different technical field than that of Meinjohanns and Komba because Ratcliffe's synthesis is a liquid-phase synthesis rather than a solid-phase synthesis, and is not used in acidic conditions for cleavage of glycopeptides from a resin. This argument is not persuasive because Komba teaches a method which makes use of protected sialic acid glycosides, and Ratcliffe also teaches protected sialic acid glycosides. Ratcliffe teaches that the use of esters other than methyl for blocking the sialoside gives a higher yield and higher anomeric purity. It is noted that the claims do not require the sialic acid protecting group to be present when the resin is cleaved, because the claim language "comprising" is open language. Furthermore, the benzyl ester prepared by Ratcliffe survives acidic conditions. See column 12, Example 1, wherein the benzyl ester survives treatment with concentrated HCl (preparation of compound 3 from compound 2).

Applicant argues that the carboxyl group of sialic acid is selectively protected under mild to neutral conditions and the carboxyl group of asparagine is not protected under those conditions. In response to applicant's argument that the references fail to

show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., selective protection of the carboxyl group of sialic acid under certain conditions) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims are not drawn to the preparation of a selectively protected asparagine-linked disialooligosaccharide and thus Applicant's argument is moot.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Monday - Friday, 7:00 - 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Layla Bland/
Examiner, Art Unit 1623

/Shaojia Anna Jiang/
Supervisory Patent Examiner
Art Unit 1623